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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	4

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/025,524	Applicant(s) KILGANNON ET AL.	
	Examiner Patricia A. Duffy	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-27* is/are pending in the application.

4a) Of the above claim(s) *18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *18-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The response and amendment of July 21, 2003 has been entered into the record. Claims 18-27 are pending.

Priority

Applicant claims benefit under 35 USC § 120 to 07/827,689 filed January 27, 1992. With respect to claims 23-26, there is no written description for the claimed monoclonal antibodies and hybridomas until the filing date of the parent Application 08/942,867. As to new claim 27, all the parent specifications lack written description for "specifically binding" anti-human ICAM-4 monoclonal antibodies as is now claimed. Further, applicants argue in the response of July 21, 2003 that "specific binding" is equated with exclusive binding as supported by a generic reference, not of record and not provided by Applicants in any IDS. This argued definition is not supported by the specification as filed.

Specification

The disclosure is objected to because of the following informalities: the specification references particular United States Applications, the status of these Applications must be updated.

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Information Disclosure Statement

The information disclosure filed March 13, 2002 has been considered. A initialed copy is enclosed.

Election/Restrictions

Applicant's election of Group II, claims 23-27 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 18-22 are withdrawn from consideration as not directed to the elected invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 27 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,773,293. Although the conflicting claims are not identical, they are not patentably distinct from each other because the monoclonal antibody species of the '293 patent clearly anticipate the genus of monoclonal antibodies recited in instant claim 27.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification fails to support the term "specifically binds" as exclusive of all other epitopes in nature as argued by Applicants in Paper No. 10, July 21, 2003. Further, the argued interpretation of "binding only to a single antigen" (i.e. exclusive binding, binding to only the polypeptide or peptide epitope of interest) is not supported by the written description at page 8, lines 2-5) or any art of record. Further, this specification fails to provide written description of any antibody that binds human ICAM-4 exclusively and distinguishes it from all other epitopes in nature. The specification fails to teach any antibody that meets this argued criteria. It is noted that the specification fails to teach that any monoclonal antibody was tested against all other epitopes in nature. Moreover, Applicants arguing that the term "specifically binds" is art recognized as exclusive binding is contradicted by the conventional teaches of the art as evidenced by Bost et al. (Immunol. Invest. 1988; 17:577-586) and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886). That an antibody "cross-reacts", i.e., binds to more than one protein sequence, does not mean that the antibody does not "specifically react" with both proteins. For example, Bost et al. describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see entire document, but especially the Abstract and Discussion). Antibodies which bound either the HIV or IL-2 derived sequence did not cross react with irrelevant peptides (e.g., "Results, page 579). Similarly, Bendayan characterizes the specific reactivity of a monoclonal antibody produced to human proinsulin and shows that although the antibody is highly specific; it is nevertheless able to bind to not only human proinsulin, but to

proinsulin from other species and even a distinct protein, glucagon, based upon conservation of an Arg-Arg dipeptide sequence in each of these molecules (see entire document). Bendayan concludes that "an antibody directed against such a sequence, although still yielding specific labeling, could reveal different molecules not related to the original antigen" (page 886, last paragraph). See also U.S. Pat. No. 6210670 (Berg) entitled "Cross-Reacting Monoclonal Antibodies Specific for E-Selectin and P-selectin". Applicant's argument attempts to limit the term "specifically reacts" in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. Consequently, it was well known in the art at the time the invention was made that antibody binding of distinct proteins was indeed specific and not exclusive as asserted by Applicants and neither the art nor Applicants specification recognize that "specific binding" is exclusive and binds "only" the indicated polypeptide. The asserted concept lacks written description in the specification as filed. Further, antibodies with these properties lack written description in the specification as filed. As such, one skilled in the art would recognize that Applicants were not in possession of such an exclusive antibody.

Claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant's referral to the deposit of the hybridoma cell lines 179I and 179H on page 44, first full paragraph of the specification is an insufficient assurance that all required deposits have been made and all the conditions of 37 CFR §1.801-1.809 have been met.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her

signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit.

Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;

2) The name and address of the depositor;

3) The date of deposit;

4) The identity of the deposit and the accession number given by the depository;

5) The date of the viability test;

6) The procedures used to obtain a sample if the test is not done by the depository; and

7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 27, the recitation of "human ICAM-4" is indefinite be specific acronyms do not confer specific structural features. The recitation of human ICAM-4 as claimed does not distinguish the recited ICAM-4

from the ICAM-4 of Brown et al (British Journal of Haematology, 101(Suppl 1):25). thus, the recitation ofICAM-4 is indefinite because it has multiple structural meanings within the protein art and while the claims are read in light of the specification the structural limitations of the specification (i.e. SEQ ID NOs) are not read into the claims.

As such, one skilled in the art would not be readily apprised of the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly

owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 27 is rejected under 35 U.S.C. 102(b) as being Oka et al (Neuroscience, 35:93-103, 1990; reference C14 on PTOL-1449) in light of Yoshihara et al (Neuron, 12:541-544, 1994; reference C21 on PTOL-1449).

Oka et al teach a monoclonal antibody and polyclonal antibody that bind the segment-specific membrane glycoprotein, telencephalin (page 94, column 1). Oka et al teach that the telecephalon protein , a specifically recognized an anti-telecephalon polyclonal antibody is present in numerous mammalian species, including mouse, rat, rabbit, cat and monkey (page 98) indicating that telencephalin in widely expressed in different mammalian species and is highly conserved, because it can be specifically recognized by the same antisera. Because the polyclonal antibody of Oka et al binds a wide variety of diverse mammalian species, it would necessarily follow that the monoclonal antibodies of Oka et al would inherently bind the instant human ICAM-4, absent convincing factual evidence to the contrary. Yoshihara et al is cited to teach that the telencephalin proteins of Oka et al and the instant human ICAM-4 are the same protein in different species. Yoshihara et al teach the cloning of full length rabbit and murine telencephalin. Although the reference is silent on referring to the encoded protein as ICAM-4, murine telencephalin and rat ICAM-4 share 95% sequence identity, both have high homology to domains II-IV of ICAM-3 (page 545 of Yoshihara) as does human ICAM-4 of the instant specification and both are expressed exclusively in the rostral part of the brain (identified as the telencephalon in Yoshihara, page 542 as the cerebral cortex and hippocampus in the instant specification) and both are most highly expressed on the dendritic processes of the neurons (page 542 of Yoshihara). For these reasons, telencephalin and ICAM-4 are the same protein in different species.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim 37 is rejected under 35 U.S.C. 102(b) as anticipated by Bailly et al (Proc. Natl. Acad. Sci. 91:5306-5310, 1994) in light of Bailly et al (Eur. J. Immunol. 25:3316-3320, 1995).

Bailly et al (Proc. Natl. Acad. Sci. 91:5306-5310, 1994) discloses a anti-human LW monoclonal antibody BS46 (inherently produced by a hybridoma, see page 5306, column 2, reagents and purification). Bailly et al (Proc. Natl. Acad. Sci. 91:5306-5310, 1994) do not call this protein ICAM-4, however Bailly et al (Eur. J. Immunol. 25:3316-3320, 1995) designate this LW protein as ICAM-4 (page 3316, column 2). Therefore, the monoclonal antibodies of Bailly et al (Proc. Natl. Acad. Sci. 91:5306-5310, 1994) inherently bind ICAM-4 as is instantly claimed, absent convincing factual evidence to the contrary.

Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oka et al (Neuroscience, 35:93-103, 1990; reference C14 on PTOL-1449) in view of Goding et al (Monoclonal antibodies, 1983, Academic Press Inc, pages 56-97) and in light of Yoshihara et al (Neuron, 12:541-544, 1994; reference C21 on PTOL-1449).

Oka et al and Yoshihara et al are set forth *supra*. While Oka et al is silent on binding to human telencephalin, Oka et al does teach that polyclonal antisera generated by immunizing with affinity purified rabbit telencephalin, was cross-reactive with several other mammalian species and thus would also be reasonably expected to bind human

telencephalin (i.e. the instant ICAM-4). Oka et al teach the purification of rabbit telencephalin using antibodies. Oka et al teach the existence of highly conserved mammalian homologues of the rabbit telencephalin protein. Oka et al teach that monoclonal antibodies were raised against rabbit telencephalin using conventional techniques (page 95, column 1, first full paragraph). Oka et al also teach that the isolation and characterization of telencephalon specific markers such as telencephalin may aid in the molecular basis of the functional and structural characteristics of the telencephalon.

Goding et al teach routine conventional steps employed in the production of monoclonal antibodies.

Yoshihara et al is cited to teach that the telencephalin proteins of Oka et al and the instant human ICAM-4 are the same protein in different species. Yoshihara et al teach the cloning of full length rabbit and murine telencephalin. Although the reference is silent on referring to the encoded protein as ICAM-4, murine telencephalin and rat ICAM-4 share 95% sequence identity, both have high homology to domains II-IV of ICAM-3 (page 545 of Yoshihara) as does human ICAM-4 of the instant specification and both are expressed exclusively in the rostral part of the brain (identified as the telencephalon in Yoshihara, page 542 as the cerebral cortex and hippocampus in the instant specification) and both are most highly expressed on the dendritic processes of the neurons (page 542 of Yoshihara). For these reasons, telencephalin and ICAM-4 are the same protein in different species.

It would have been *prima facie* obvious to isolate human telencephalin using the broadly reactive polyclonal antisera of Oka et al and use the isolated human telencephalin in the method of Goding et al to make anti-human telencephalin monoclonal antibodies because Oka et al teach that mammalian homologues of rabbit telencephalin are present in other mammalian species including mouse, rat, rabbit, cat, and monkey (page 98) and one of ordinary skill in the art would reasonable expect to isolate human telencephalin and make monoclonal antibodies using conventional isolation and screening procedures set forth in

Oka et al and Goding et al. One of ordinary skill in the art would have a reasonable expectation of success give that Oka et al has demonstrated the isolation of a anti-rabbit monoclonal antibody 271A6. Further, one would have been motivated to make anti-human telencephalin monoclonal antibodies because of the well accepted, art recognized advantages of monoclonal antibodies, including an unlimited supply of high quality antibodies with specificity and reproducible binding characteristics and Oka et al teach that characterization of the telencephalon specific markers such as telencephalin may aid in the delineation of the functional and structural characteristics of the telencephalon.

Status of the Claims

Claims 23-27 stand rejected. Claims 18-22 are withdrawn from consideration as drawn to a non-elected invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 703-305-7555. The examiner can normally be reached on M-F 9:30pm-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645

Patricia A. Duffy, Ph.D.

November 16, 2003